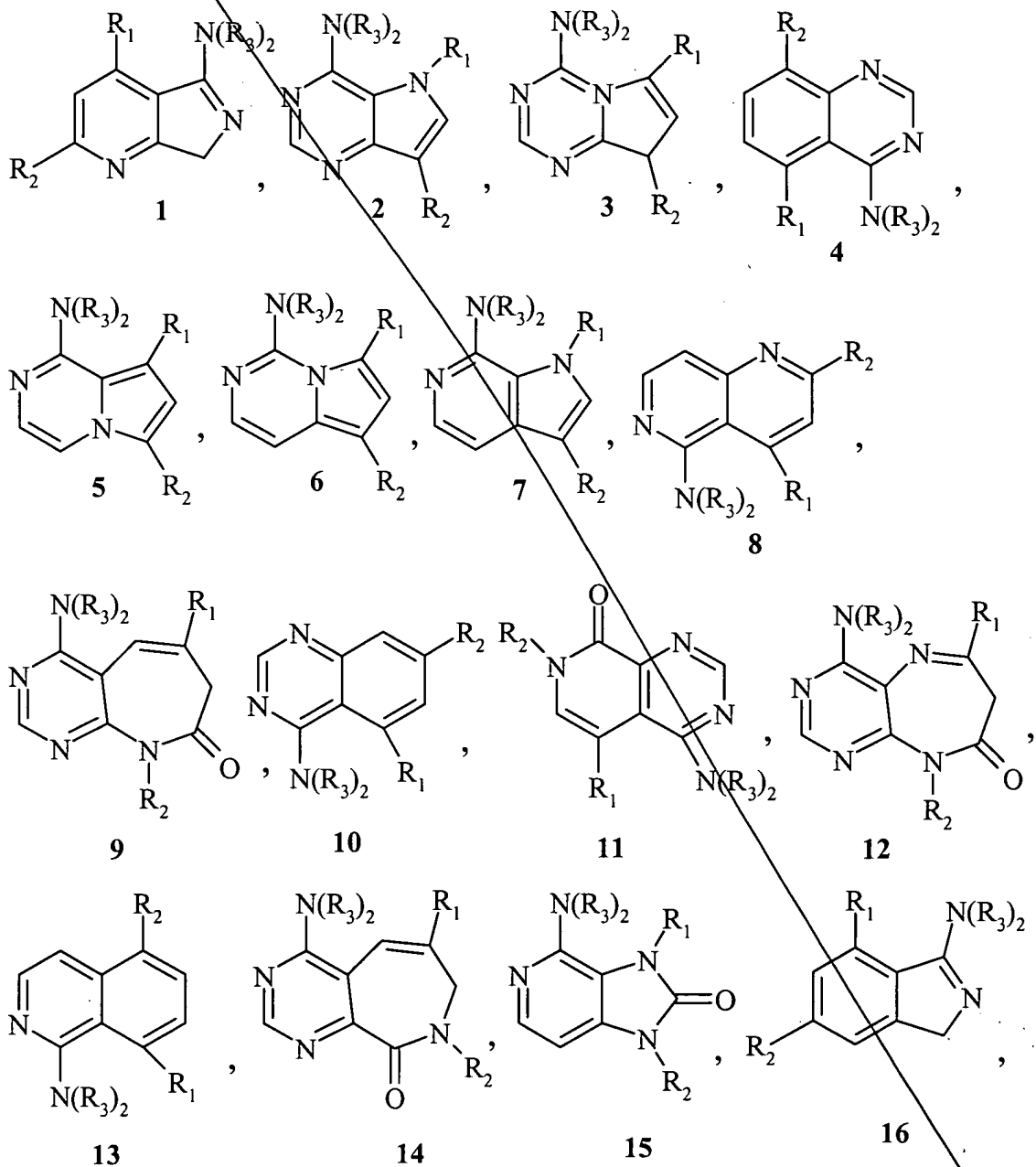


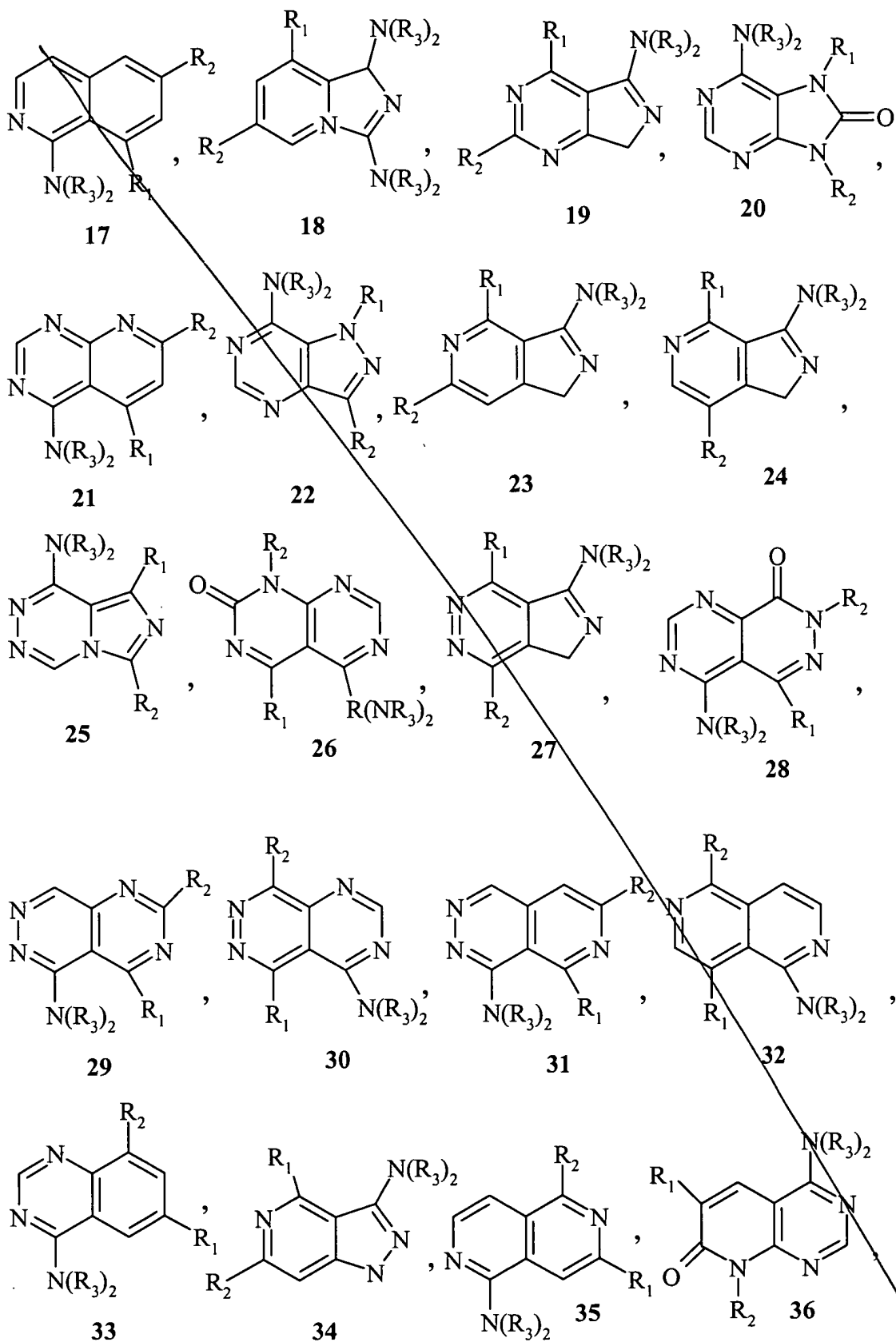
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CLAIMS

We claim:

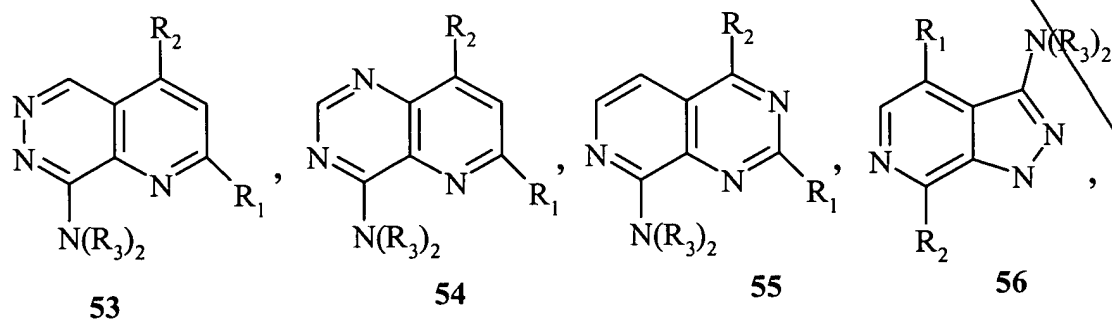
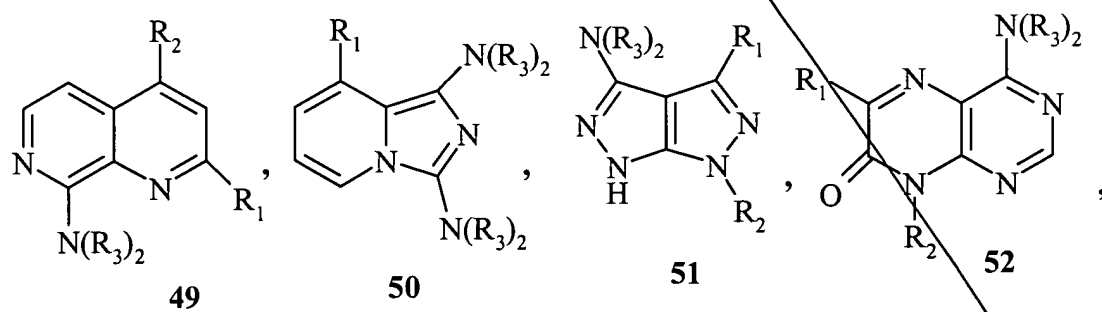
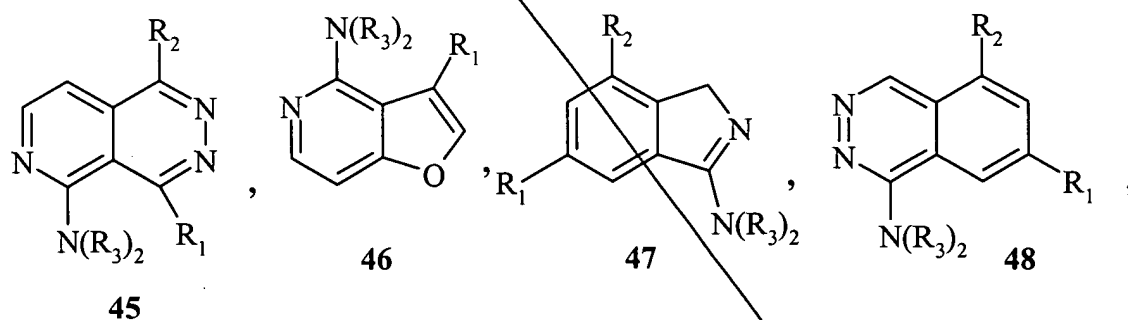
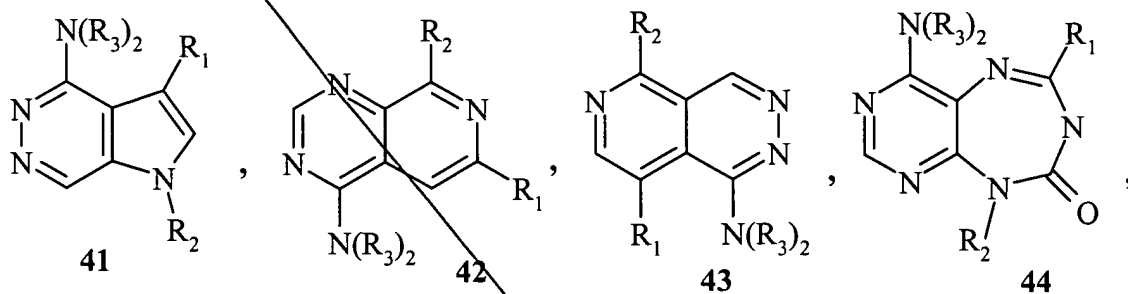
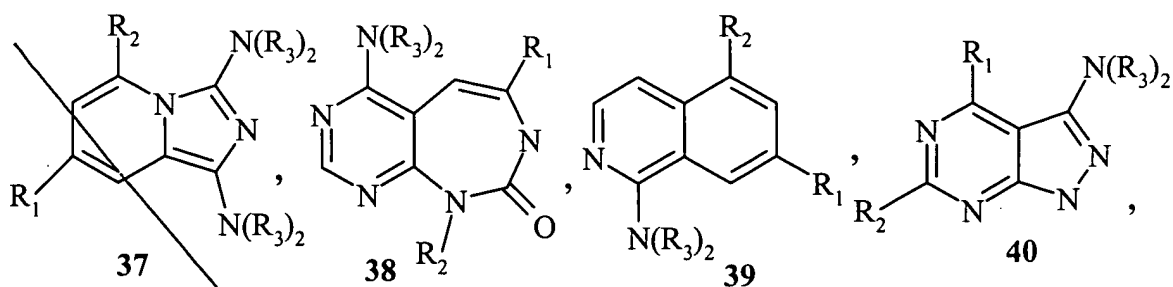
- 5 1. A compound of Formula (I), the racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof, selected from the group consisting of

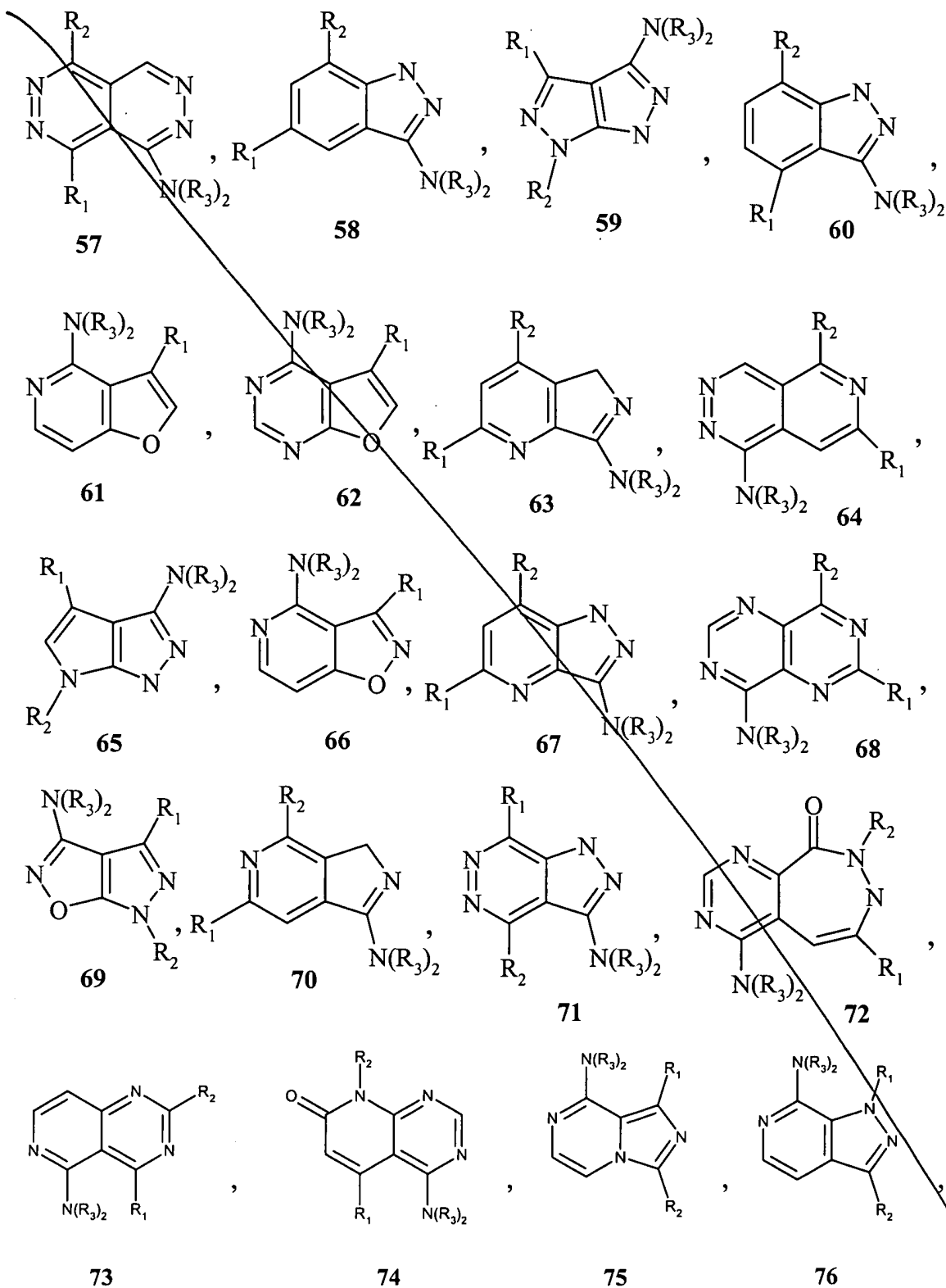


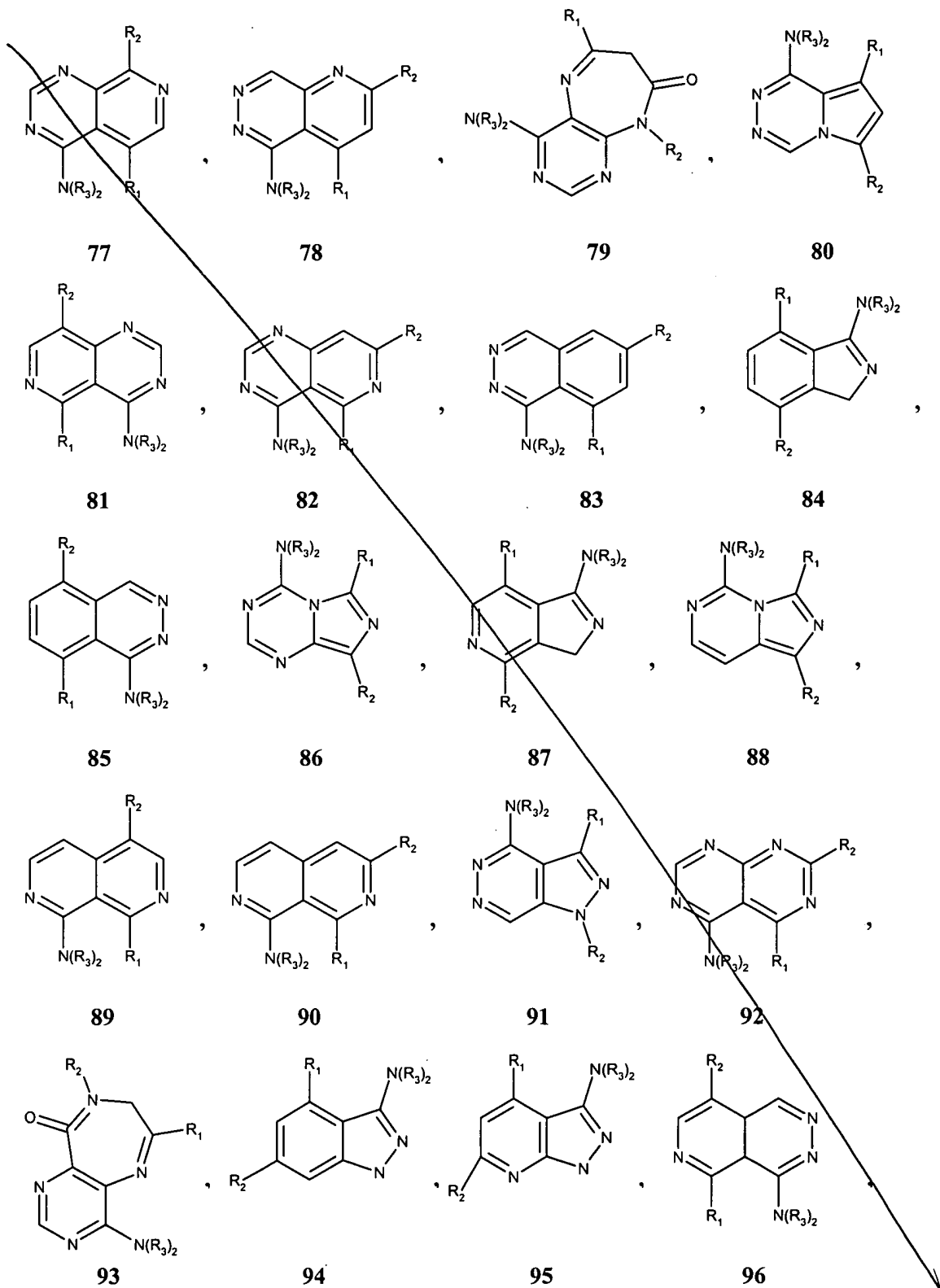
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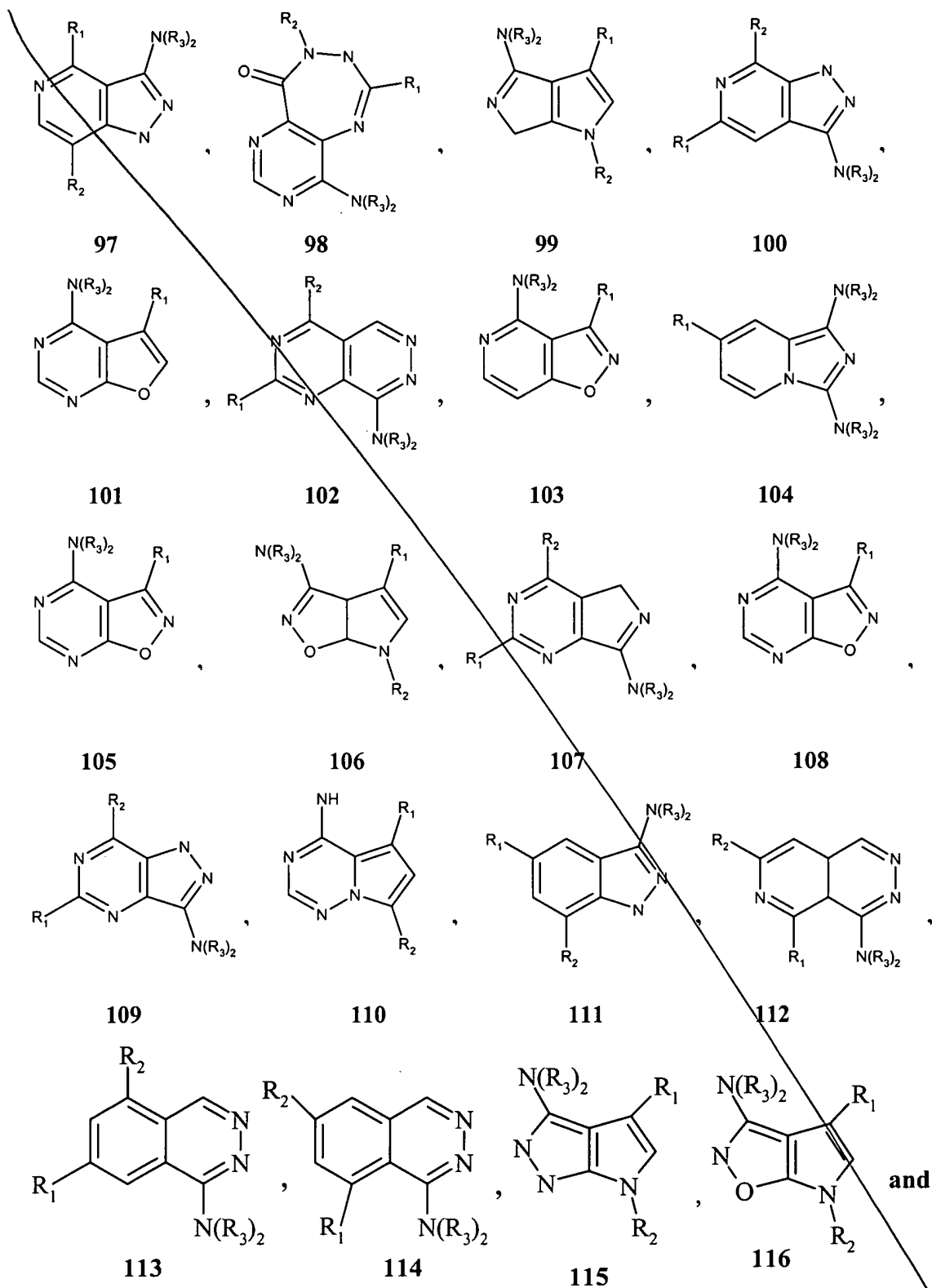


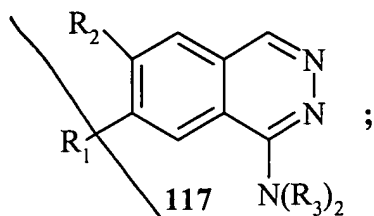
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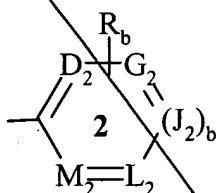
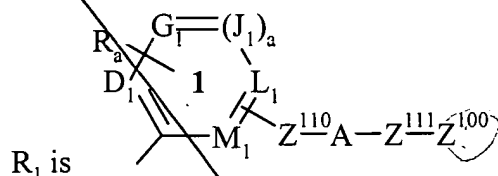
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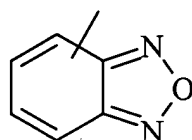
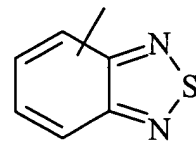


wherein:



where Z¹⁰⁰ is or a group optionally substituted with R_b selected from the group consisting of cycloalkyl, naphthyl, tetrahydronaphthyl,

benzothienyl, furanyl, thienyl, benzoxazolyl, benzothiazolyl,



, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidiny, pyrazolyl, pyrrolyl, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, benzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z¹¹⁰ is a covalent bond, or an optionally substituted (C₁-C₆) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO₂, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z¹¹¹ is a covalent bond, an optionally substituted (C₁-C₆) or an optionally substituted

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 $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO₂, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_i each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, -NO₂, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z¹⁰⁵-C(O)N(R)₂, -Z¹⁰⁵-N(R)-C(O)-Z²⁰⁰, -Z¹⁰⁵-N(R)-S(O)₂-Z²⁰⁰, -Z¹⁰⁵-N(R)-C(O)-N(R)-Z²⁰⁰, R_c and CH₂OR_c;

where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, -CH₂-NR_dR_e, -W-(CH₂)_t-NR_dR_e, -W-(CH₂)_t-Oalkyl, -W-(CH₂)_t-S-alkyl, or -W-(CH₂)_t-OH;

Z¹⁰⁵ for each occurrence is independently a covalent bond or (C₁-C₆);

Z²⁰⁰ for each occurrence is independently a substituted or unsubstituted (C₁-C₆), substituted or unsubstituted phenyl or substituted or unsubstituted -(C₁-C₆)-phenyl;

25 R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO₂-alkyl; or R_d, R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring; t for each occurrence is independently an integer from 2 to 6; W for each occurrence is independently a direct bond or O, S, S(O), S(O)₂, or NR_f,
 30 wherein R_f for each occurrence is independently H or alkyl;

or R_i is a substituted or unsubstituted carbocyclic or heterocyclic ring fused

with

ring 2;

R_3 is hydrogen, hydroxy, substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy;

A is -O-; -S-; -S(O)_p-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -N(SO₂R)-; -CH₂O-; -CH₂S-; -CH₂N(R)-; -CH(NR)-; -CH₂N(C(O)R)-; -CH₂N(C(O)OR)-; -CH₂N(SO₂R)-; -CH(NHR)-; -CH(NHC(O)R)-; -CH(NHSO₂R)-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR)-; -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; -N(R)S(O)_p-; -OC(O)N(R)-; -N(R)-C(O)-(CH₂)_n-N(R)-; -N(R)C(O)O-; -N(R)-(CH₂)_{n+1}-C(O)-; -S(O)_pN(R)-; -O-(CR₂)_{n+1}-C(O)-; -O-(CR₂)_{n+1}-O-; -N(C(O)R)S(O)_p-; -N(R)S(O)_pN(R)-; -N(R)-C(O)-(CH₂)_n-O-; -C(O)N(R)C(O)-; -S(O)_pN(R)C(O)-; -OS(O)_pN(R)-; -N(R)S(O)_pO-; -N(R)S(O)_pC(O)-; -SO_pN(C(O)R)-; -N(R)SO_pN(R)-; -C(O)O-; -N(R)P(OR_g)O-; -N(R)P(OR_g)-; -N(R)P(O)(OR_g)O-; -N(R)P(O)(OR_g)-; -N(C(O)R)P(OR_g)O-; -N(C(O)R)P(OR_g)-; -N(C(O)R)P(O)(OR_g)O-; or -N(C(O)R)P(OR_g)-;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_g for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2;

or in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_g together form a five- or six-membered heterocyclic ring; or

A is NRSO₂ and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or six-membered heterocyclic ring fused to ring 1;

R_2 is -Z¹⁰¹-Z¹⁰²;

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 ~~Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted or unsubstituted phenyl group;~~

~~Z^{102} is hydrogen, a substituted or unsubstituted alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted, saturated or unsaturated heterocyclic group, or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group;~~

~~said substituted heterocyclic or substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of~~
10 ~~hydroxyl, cyano, substituted or unsubstituted alkoxy, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido; substituted or unsubstituted amino, oxo, a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more nitrogen atoms, one or more oxygen atoms or a~~
15 ~~combination thereof;~~

~~wherein said nitrogen atoms are independently optionally substituted by a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; or~~

~~R_2 is of the formula B-E, wherein B is a substituted or unsubstituted cycloalkyl,~~
20 ~~substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, hydroxy, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted~~
25 ~~or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted azacycloalkyl, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted~~
30 ~~heteroarylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino or substituted or unsubstituted aryl;~~

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a is 1 and D₁, G₁, J₁, L₁ and M₁ are each independently selected from the group consisting of CR_a and N, provided that at least two of D₁, G₁, J₁, L₁ and M₁ are CR_a; or

a is 0, and one of D₁, G₁, L₁ and M₁ is NR_a, one of D₁, G₁, L₁ and M₁ is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

b is 1 and D₂, G₂, J₂, L₂ and M₂ are each independently selected from the group consisting of CR_a and N, provided that at least two of D₂, G₂, J₂, L₂ and M₂ are CR_a; or

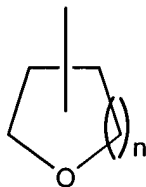
10 b is 0, and one of D₂, G₂, L₂ and M₂ is NR_a, one of D₂, G₂, L₂ and M₂ is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6.

15 2. The compound of Claim 1 wherein R₃ is H; R₁ for each occurrence is independently selected from the group consisting of F, Cl, Br, I, CH₃, NO₂, OCF₃, OCH₃, CN, CO₂CH₃, CF₃, -CH₂NR_dR_e, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, and substituted or unsubstituted styryl.

25 3. The compound of Claim 1 wherein R₃ is H; R_a for each occurrence is independently selected from the group consisting of F, Cl, Br, I, CH₃, NO₂, OCF₃, OCH₃, CN, CO₂CH₃, CF₃, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, and substituted or unsubstituted styryl.

4. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

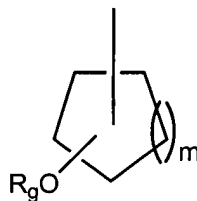


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wherein n is 1, 2 or 3.

5. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

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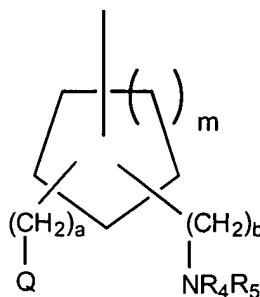
wherein m is 0, 1, 2 or 3 and

R_9 is H or $-(CH_2)_pN(R_4)R_5$, wherein p is an integer from 2 to 6 and R_4 and R_5 are each, independently, H, azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted moiety selected from the group consisting of alkyl, alkoxy, amino, aryl, heteroaryl and heterocycloalkyl group or R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group.

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6. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



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wherein m is 0, 1, 2 or 3

a and b are each, independently, an integer from 0 to 6;

Q is $-OR_6$ or $-NR_4R_5$;

each R_4 and R_5 is, independently, H, azabicycloalkyl or Y-Z, wherein Y is

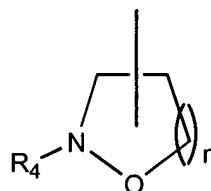
5 selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, amino, aryl, heteroaryl or heterocycloalkyl group or

10 R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group; and

R_6 is hydrogen or a substituted or unsubstituted alkyl group.

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7. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

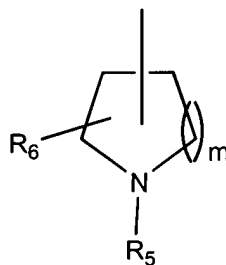


wherein n is 1, 2 or 3; and

R_4 is H, azabicycloalkyl or Y-Z, wherein Y is selected

from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group.

8. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein

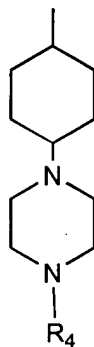
m is 0, 1, 2 or 3;

R_5 is H, azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of a covalent bond, $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, $-(CH_2)_qC(O)-$, $-C(O)(CH_2)_q-$ and $-(CH_2)_qS(O)_r-$, where the alkyl portion of $-(CH_2)_q-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, $-(CH_2)_qC(O)-$, $-C(O)(CH_2)_q-$ and $-(CH_2)_qS(O)_r$ is optionally substituted by a halogen, hydroxy or an alkyl group;

wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or Y and Z together are a natural or unnatural amino acid, which may be mono- or di-alkylated at the amine nitrogen; and

R_6 represents one or more substituents each independently selected from the group consisting of hydrogen, hydroxy, oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heterocyclylcarbonyl, substituted or unsubstituted aminoalkyl and substituted or unsubstituted arylalkyl; provided that the carbon atoms adjacent to the nitrogen atom are not substituted by a hydroxy group.

9. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

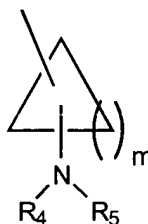


wherein R_4 is H, substituted or unsubstituted alkyl, substituted or unsubstituted azabicycloalkyl or $Y-Z$, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6, and r is 0, 1 or 2; and Z is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl

or substituted or unsubstituted heterocycloalkyl.

10. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

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wherein

m is an integer from 1 to 6; and

R_4 and R_5 are each, independently, H, substituted or unsubstituted

azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -

$C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$,

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and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z

is a substituted or unsubstituted alkyl, substituted or unsubstituted amino,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or

substituted or unsubstituted heterocycloalkyl group; or

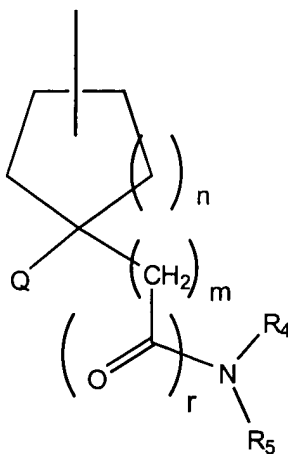
R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6

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or 7-membered, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterobicyclic group.

11. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

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wherein

n is an integer from 0 to 4;

r is 0 and m is an integer from 1 to 6; or

5 r is 1 and m is an integer from 0 to 6;

Q is $-OR_6$ or $-NR_4R_5$;

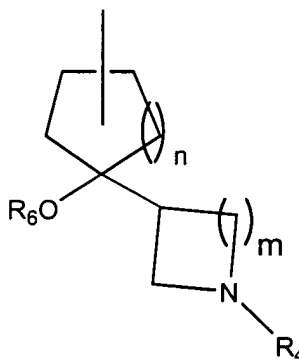
each R_4 and R_5 is, independently, H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$

10 ; q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

15 R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group; and R_6 is hydrogen or a substituted or unsubstituted alkyl group.

12. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

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25

n is an integer from 0 to 4;

m is an integer from 0 to 6;

R_4 is H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an

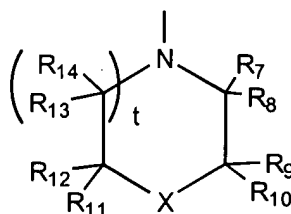
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integer from 0 to 6; and r is 0, 1 or 2; and Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; and R_6 is hydrogen or a substituted or unsubstituted alkyl group.

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13. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula

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wherein

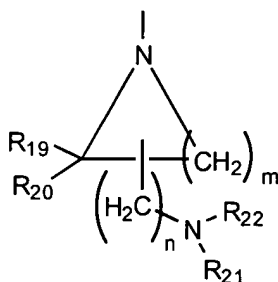
- R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} and R_{14} are each, independently, lower alkyl or hydrogen; or at least one pair of substituents R_7 and R_8 ; R_9 and R_{10} ; R_{11} and R_{12} ; or R_{13} and R_{14} together are an oxygen atom; or at least one of R_7 and R_9 is cyano, CONHR_{15} , COOR_{15} , $\text{CH}_2\text{OR}_{15}$ or $\text{CH}_2\text{NR}_{15}(\text{R}_{16})$, wherein R_{15} and R_{16} are each, independently, H, azabicycloalkyl or V-L, wherein V is selected from the group consisting of $-\text{C}(\text{O})-$, $-(\text{CH}_2)_p-$, $-\text{S}(\text{O})_2-$, $-\text{C}(\text{O})\text{O}-$, $-\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S}(\text{O})_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R_{15} , R_{16} and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or a substituted or unsubstituted heterobicyclic group;
- X is O, S, SO, SO_2 , CH_2 , CHOR_{17} or NR_{17} , wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $-\text{C}(\text{NH})\text{NH}_2$, $-\text{C}(\text{O})\text{R}_{17}$, or $-\text{C}(\text{O})\text{OR}_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

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t is 0 or 1.

14. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocycle of the formula

5



10

wherein

R_{19} and R_{20} are each, independently, hydrogen or lower alkyl; or R_{19} and R_{20} together are an oxygen atom;

15

R_{21} and R_{22} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -SO₂NH-, -CONH-, (CH₂)_qO-, -(CH₂)_qNH-, and -(CH₂)_qS(O)_r-; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

20

R_{21} , R_{22} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group;

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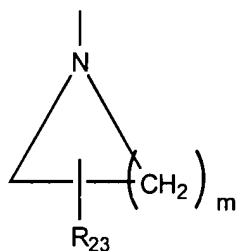
m is an integer from 1 to 6; and

n is an integer from 0 to 6.

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15. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula

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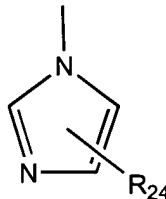


wherein

m is an integer from 1 to 6; and

- 10 R_{23} is CH_2OH , NRR' , $\text{C(O)NRR}'$ or COOR , wherein R and R' are each, independently, hydrogen or substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl.

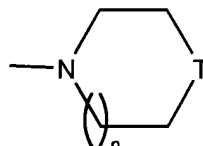
- 15 16. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula



- 20 wherein R_{24} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl, carboxyl, cyano, C(O)OR_{25} , $\text{CH}_2\text{OR}_{25}$, $\text{CH}_2\text{NR}_{26}\text{R}_{27}$ or C(O)NHR_{26} , wherein R_{25} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterocycloaryl; and R_{26} and R_{27} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of $-\text{C(O)}-$, $-(\text{CH}_2)_p-$, $-\text{S(O)}_2-$, $-\text{C(O)O}-$, $-\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S(O)}_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or
- 25
- 30

unsubstituted heterocycloalkyl; or R_{26} , R_{27} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group.

17. The compound of Claim 10 wherein at least one of R_4 and R_5 is of the formula
5 Y-Z, wherein Z is of the formula



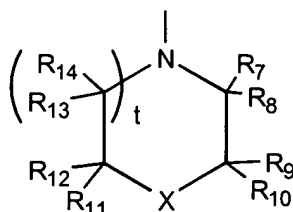
- 10 wherein

T is C(O), S, SO, SO₂, CHOR or NR, wherein R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; and
n is 0, 1 or 2.

15

18. The compound of Claim 10 wherein at least one of R_4 and R_5 is of the formula
Y-Z, wherein Z is of the formula $-N(R_{28})R_{29}$, wherein R_{28} and R_{29} are each,
independently, substituted or unsubstituted carboxyalkyl, substituted or
unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl,
20 substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted
alkylcarbonyl or substituted or unsubstituted cyanoalkyl; or
 R_{28} and R_{29} , together with the nitrogen atom, form a five- or six-membered
substituted or unsubstituted heterocyclic group.

- 25 19. The compound of Claim 11 wherein R_4 , R_5 and the nitrogen atom together form a heterocycle of the formula



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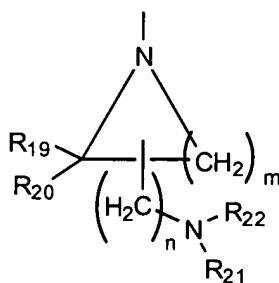
wherein

$R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}$ and R_{14} are each, independently, lower alkyl or hydrogen; or at least one pair of substituents R_7 and R_8 ; R_9 and R_{10} ; R_{11} and R_{12} ; or R_{13} and R_{14} together are an oxygen atom; or at least one of R_7 and R_9 is cyano, CONHR₁₅, COOR₁₅, CH₂OR₁₅ or CH₂NR₁₅(R₁₆), wherein R₁₅ and R₁₆ are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -SO₂NH-, -CONH-, (CH₂)_qO-, -(CH₂)_qNH-, and -(CH₂)_qS(O)_r-; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R₁₅, R₁₆ and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group;

X is O, S, SO, SO₂, CH₂, CHOR₁₇ or NR₁₇, wherein R₁₇ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, -C(NH)NH₂, -C(O)R₁₈, or -C(O)OR₁₈, wherein R₁₈ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

t is 0 or 1.

20. The compound of Claim 11 wherein R₄, R₅ and the nitrogen atom together form a heterocycle of the formula



wherein

R_{19} and R_{20} are each, independently, hydrogen or lower alkyl; or R_{19} and R_{20} together are an oxygen atom;

5 R_{21} and R_{22} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_rS(O)-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_{21} , R_{22} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group;

m is an integer from 1 to 6; and

15 n is an integer from 0 to 6.

21. The compound of Claim 11 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula



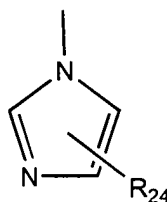
25 wherein

m is an integer from 1 to 6; and

R_{23} is CH_2OH , NRR' , $C(O)NRR'$ or $COOR$, wherein R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group.

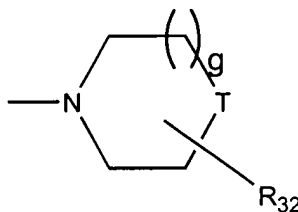
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22. The compound of Claim 11 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula



- wherein R_{24} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl, carboxyl, cyano, $C(O)OR_{25}$, CH_2OR_{25} , $CH_2NR_{26}R_{27}$ or $C(O)NHR_{26}$, wherein R_{25} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterocycloaryl group; and R_{26} and R_{27} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of $-C(O)-$, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or R_{26} , R_{27} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group.
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23. The compound of Claim 11 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula



wherein

- 30 g is 0 or 1;

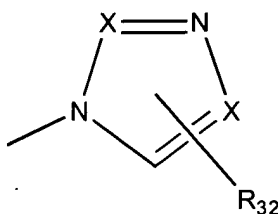
T is C(O), O, S, SO, SO₂, CH₂, CHOR₁₇ or NR₁₇, wherein R₁₇ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, -C(NH)NH₂, -C(O)R₁₈, or -C(O)OR₁₈, wherein R₁₈ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

R₃₂ is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl.

24. The compound of Claim 11 wherein at least one of R₄ and R₅ is of the formula Y-Z, wherein Z is of the formula -N(R₂₈)R₂₉, wherein R₂₈ and R₂₉ are each, independently, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted alkoxy carbonylalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted cyanoalkyl; or R₂₈ and R₂₉, together with the nitrogen atom, form a five- or six-membered substituted or unsubstituted heterocyclic group.

25. The compound of Claim 8 wherein R₅ is Y-Z, wherein Z is of the formula N(R₃₀)R₃₁, wherein R₃₀ and R₃₁ are each, independently, hydrogen, alkyl, alkoxy carbonyl, alkoxyalkyl, hydroxyalkyl, aminocarbonyl, cyano, alkylcarbonyl or arylalkyl.

26. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



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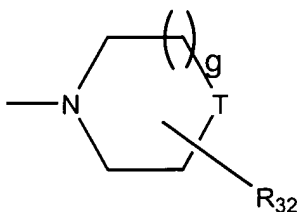
wherein

each X is, independently, CH or N; and

- 10 R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxy alkyl, substituted or unsubstituted hydroxy alkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkyl carbonyl or substituted or unsubstituted aryl alkyl group.

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27. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



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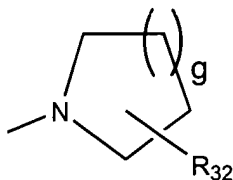
wherein

g is 0 or 1;

- 25 T is O, S, SO, SO₂, CH₂, CHOR₁₇ or NR₁₇, wherein R₁₇ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted aryl alkyl, C(O)NH₂, -C(NH)NH₂, -C(O)R₁₇, or -C(O)OR₁₈, wherein R₁₈ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted aryl alkyl; and
- 30 R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxy alkyl,

substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

- 5 28. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula

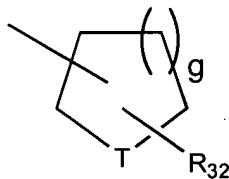


10 wherein

g is 0, 1 or 2; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

- 15 29. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



20 wherein

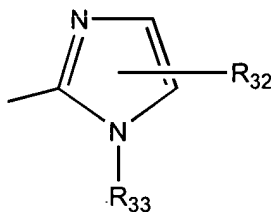
T is $C(O)$, O, S, SO, SO_2 , CH_2 , $CHOR_{17}$ or NR_{17} , wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, aryl, arylalkyl, $-C(NH)NH_2$, $-C(O)R_{18}$, or $-C(O)OR_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; g is 0 or 1; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl,

25 30

substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

- 5 30. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



10

wherein

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl,

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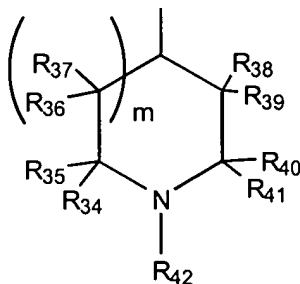
substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, alkylcarbonyl, substituted or unsubstituted thioalkoxy or substituted or unsubstituted arylalkyl; and

R_{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl,

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substituted or unsubstituted aminocarbonyl, perhaloalkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl.

31. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



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wherein

m is 0 or 1;

R_{34} , R_{35} , R_{36} , R_{37} , R_{38} , R_{39} , R_{40} and R_{41} are each, independently, methyl or hydrogen; or at least one pair of substituents R_{34} and R_{35} ; R_{36} and R_{37} ; R_{38} and R_{39} ; or R_{40} and R_{41} together are an oxygen atom; and

5 R_{42} is H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -C(O)-, $-(CH_2)_p-$, $-S(O)_2-$, -C(O)O-, -SO₂NH-, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_{42} is of the formula



wherein

20 u is 0 or 1;

R_{43} , R_{44} , R_{45} , R_{46} , R_{47} , R_{48} , R_{49} and R_{50} are each, independently, methyl or hydrogen;

or at least one pair of substituents R_{43} and R_{44} ; R_{45} and R_{46} ; R_{47} and R_{48} ;

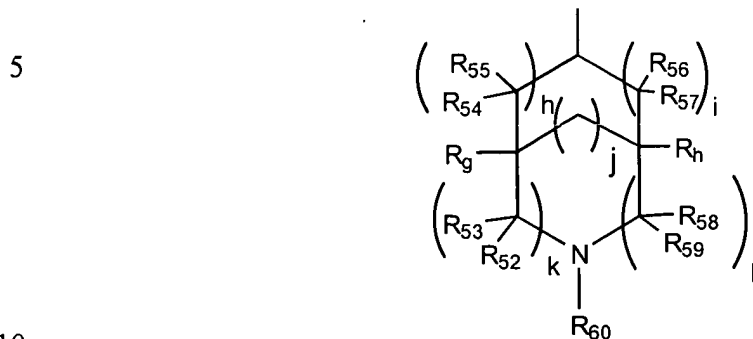
or R_{49} and R_{50} together are an oxygen atom; and

25 R_{51} is H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$, $-S(O)_2-$, -C(O)O-, -SO₂NH-, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or

30

unsubstituted heterocycloalkyl.

32. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



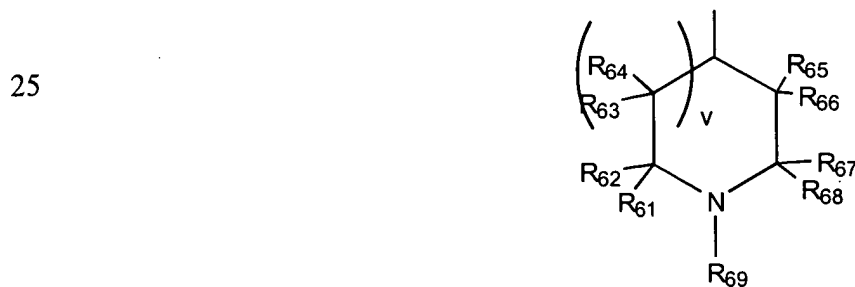
wherein

h, i, j, k and l are independently 0 or 1;

$R_{52}, R_{53}, R_{54}, R_{55}, R_{56}, R_{57}, R_{58}, R_{59}, R_g$ and R_h are each, independently, methyl or hydrogen; or at least one pair of substituents R_{52} and R_{53} ; R_{54} and R_{55} ; R_{56} and R_{57} ; or R_{58} and R_{59} together are an oxygen atom; and

R_{60} is H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or

R_{60} is of the formula



wherein

v is 0 or 1;

R_{61} , R_{62} , R_{63} , R_{64} , R_{65} , R_{66} , R_{67} and R_{68} are each, independently, lower alkyl or hydrogen; or at least one pair of substituents R_{61} and R_{62} ; R_{63} and R_{64} ; R_{65} and R_{66} ; and R_{67} and R_{68} together are an oxygen atom; and R_{69} is H, substituted or unsubstituted azabicycloalkyl or V-1, wherein V is selected from the group consisting of $-C(O)-$, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl.

Sub C2
33. A method of inhibiting one or more protein kinase activity in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

34. The method of Claim 33 wherein said protein kinase is selected from the group consisting of KDR, FGFR-1, PDGFR β , PDGFR α , IGF-1R, c-Met, Flt-1, Flt-4, TIE-2, TIE-1, Lck, Src, fyn, Lyn, Blk, hck, fgr and yes.

Sub C3
35. A method of affecting hyperproliferative disorders in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

36. A method of affecting angiogenesis in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

37. The method of Claim 33 wherein the protein kinase is a protein serine/threonine kinase or a protein tyrosine kinase.

Sub
C4

38. A method of treating one or more ulcers in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

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39. The method of Claim 38 wherein the ulcer or ulcers are caused by a bacterial or fungal infection; or the ulcer or ulcers are Mooren ulcers; or the ulcer or ulcers are a symptom of ulcerative colitis.

Sub
C5

10 40. A method of treating a condition in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient, wherein said condition is an ocular condition, a cardiovascular condition, a cancer, Crow-Fukase (POEMS) syndrome, a diabetic condition, sickle cell
15 anaemia, chronic inflammation, systemic lupus, glomerulonephritis, synovitis, inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, graft rejection, Lyme disease, sepsis, von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease, polycystic kidney disease, fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity
20 syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease, asthma or edema following burns, trauma, radiation, stroke, hypoxia, ischemia, ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, endometriosis, or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa or toxoplasmosis.

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41. The method of Claim 40 wherein the ocular condition is ocular or macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser treatment complications, conjunctivitis, Stargardt's disease, Eales disease, retinopathy or
30 macular degeneration.

42. The method of Claim 40 wherein the cardiovascular condition is atherosclerosis, restenosis, ischemia/reperfusion injury, vascular occlusion or carotid obstructive disease.

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43. The method of Claim 40 wherein the cancer is a solid tumor, a sarcoma, fibrosarcoma, osteoma, melanoma, retinoblastoma, a rhabdomyosarcoma, glioblastoma, neuroblastoma, teratocarcinoma, an hematopoietic malignancy, Kaposi's sarcoma, Hodgkin's disease, lymphoma, myeloma, leukemia or malignant ascites.

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44. The method of Claim 40 wherein the diabetic condition is insulin-dependent diabetes mellitus glaucoma, diabetic retinopathy or microangiopathy.

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45. A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolite thereof.

Sub
C6

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46. The method of Claim 36 wherein the compound or a physiologically acceptable salt, prodrug or biologically active metabolite thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.

47. The method of Claim 34 wherein the protein kinase is Tie-2.

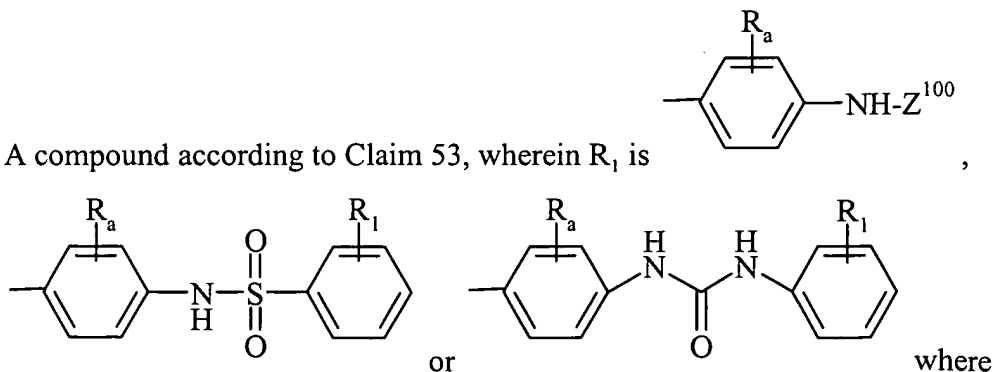
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48. The method of Claim 46 wherein the compound of Formula I, or physiologically acceptable salt, prodrug or biologically active metabolite thereof, is administered in combination with a pro-angiogenic growth factor.

Sub
C7

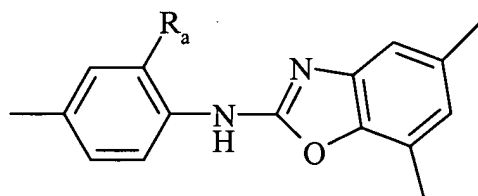
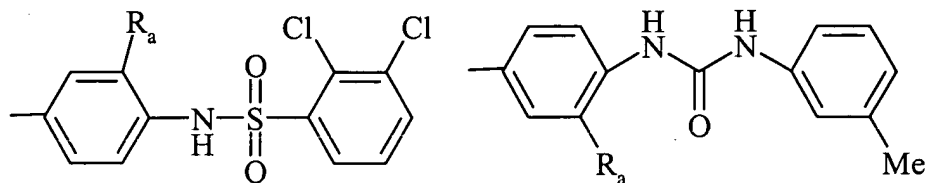
49. The method of Claim 48 wherein the pro-angiogenic growth factor is selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, VEGF-E, HGF, FGF-1, FGF-2, derivatives thereof and antiidotypic antibodies.
50. The method of Claim 46 wherein the patient is suffering from anemia, ischemia, infarct, transplant rejection, a wound, gangrene or necrosis.
51. The method of Claim 33 wherein the protein kinase activity is involved in T cell activation, B cell activation, mast cell degranulation, monocyte activation, the potentiation of an inflammatory response or a combination thereof.
52. A compound according to Claim 1, wherein R_3 is H;
 R_2 is $-Z^{101}-Z^{102}$ where Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted phenyl group; and
 Z^{102} is hydrogen, a substituted or unsubstituted alkyl group or a substituted or unsubstituted, saturated or unsaturated heterocyclic group.
53. A compound according to Claim 52, wherein Z^{101} is selected from the group consisting of $-CH_2-C(O)O-$, $-CH_2-C(O)-$, $-CH_2-C(O)-NH-$, $-CH_2-C(O)-N(Me)-$, $-CH(Me)-C(O)O-$, $-(CH_2)_3-C(O)O-$, $-CH(Me)-C(O)-NH-$, and $-(CH_2)_3-C(O)-NH-$;
 Z^{102} is selected from the group consisting of hydrogen, methyl, ethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, 2-phenyl-2-hydroxyethyl, morpholino, piperazinyl, N-methylpiperazinyl and 2-hydroxymethylpyrrolidinyl.

54. A compound according to Claim 53, wherein R_1 is



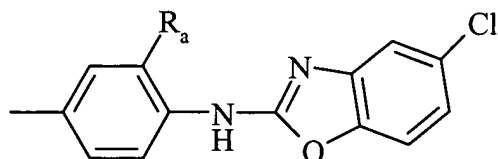
Z^{100} is a substituted or unsubstituted benzoxazolyl or a substituted or unsubstituted benzthiazolyl.

55. A compound according to Claim 8, 9, 10 or 53, wherein R_1 is



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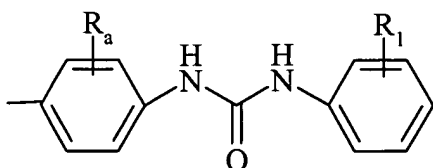
or



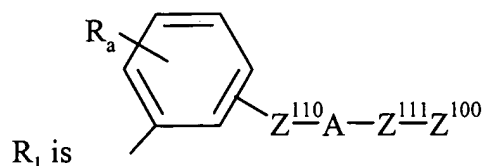
where there is only one R_a and it is H or F.

56. A compound according to Claim 52, wherein Z^{101} is a covalent bond; and Z^{102} is an optionally substituted pyridyl.

57. A compound according to Claim 56, wherein R_1 is



58. A compound according to Claim 1, wherein R_3 is H;
 R_2 is cyclopentyl; and



59. A compound according to Claim 58, wherein
 Z^{110} is hydrogen;
- 5 A is O; and Z^{100} is optionally substituted phenyl, furanyl or thienyl, where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, COOH, NO₂, OMe, -COOMe, OCF₃ and CF₃.
60. A compound according to Claim 58, wherein
 Z^{110} is hydrogen;
 A is -O-, -O-(CR₂)_n-C(O)- or -O-(CR₂)_n-O-;
 n for each occurrence is 0 to 3;
 Z^{100} is an optionally substituted group selected from the group consisting of cyclohexyl, phenyl, tetrahydropyranyl, tetrahydrofuranyl, isoxazolyl and piperidinyl; where Z^{100} is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkoxy, halo, hydroxy and alkoxycarbonyl.
- 10
61. A compound according to Claim 58, wherein R² is an optionally substituted group selected from the group consisting of cyclobutyl and cyclohexyl.
- 20
62. A compound according to Claim 61, wherein R² is optionally substituted with one or more substituents selected from the group consisting of hydroxy, alkyl, hydroxyalkyl, carboxyalkyl and phenylalkoxyalkyl.
- 25
63. A compound according to Claim 62, wherein R₁ is 4-phenoxyphenyl.
64. A compound according to Claim 6 wherein

m is 2; a is 0; R_6 is H; b is 1 or 2; and R_4 and R_5 are each hydrogen.

65. A compound according to Claim 8, wherein

m is 0, 1 or 2; R_6 is hydrogen; R_5 is H or Y-Z;

5 where Y is a covalent bond, $-C(O)-$, $-(CH_2)_qO-$, $-(CH_2)_q-$, $-(CH_2)_qC(O)-$ or $-C(O)(CH_2)_q-$, where the alkyl portion of $-(CH_2)_qO-$, $-(CH_2)_q-$, $-(CH_2)_qC(O)-$ and $-C(O)(CH_2)_q-$ is optionally substituted by a halogen, hydroxy or an alkyl group; and

10 Z is hydrogen, alkyl, optionally substituted alkyl, alkoxyalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, or optionally substituted amino.

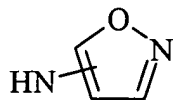
66. A compound according to Claim 65, wherein

15 Z is hydrogen, methyl, ethyl, hydroxymethyl, methoxyethyl, N-methyl-piperidinyl, (t-butoxycarbonyl)(hydroxy)-piperidinyl, hydroxypiperidinyl, (hydroxymethyl)piperidinyl, (hydroxy)(methyl)-piperidinyl, morpholino, (methoxyethyl)piperizinyl, methylpiperizinyl, 4-piperidinylpiperidinyl, imidazolyl, methylimidazolyl, N-methylamino, N,N-dimethylamino, N-isopropylamino, N,N-diethylamino, 2,3-dihydroxypropylamino, 2-

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hydroxyethylamino, 3-hydroxypropylamino, methoxyethylamino, ethoxycarbonylmethylamino, phenylmethylamino, N-methyl-N-methoxyamino,

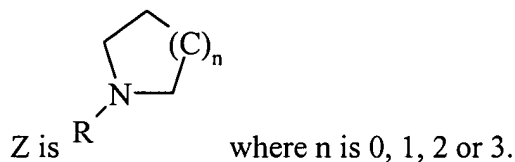
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, furanylmethylamino, piperidinyethylamino, N-(2-N,N-dimethylaminoethyl)-N-methylamino, 2-N,N-dimethylaminoethylamino, N-methyl-N-(N-methylpiperidin-4-yl)amino, 2-morpholino-ethylamino, 3-morpholino-propylamino, 3-imidazolylpropylamino, or 3-(2-

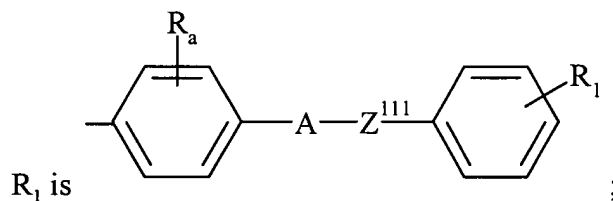
oxopyrrolidinyl)propylamino.

67. A compound according to Claim 8, wherein m is 2; R_5 is $Y-Z$; Y is $-C(O)-$; and



5

68. A compound according to Claim 9, wherein
 R_4 is hydrogen or methyl;



A is selected from the group consisting of O , $-N(R)-$ and $-N(R)C(O)-$;

Z^{111} is $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$;

R is hydrogen or alkyl;

n is 0 to 5;

R_a is one or more substituents each independently selected from the group consisting of H , OH , F , Cl , methyl and methoxy; and

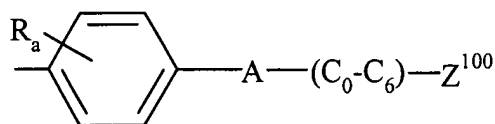
R_b is one or more substituents each independently selected from the group consisting of H , CN , F , CF_3 , OCF_3 , methyl, methoxy and an optionally substituted amino group;

where said amino group is optionally substituted with one or two groups each independently selected from the group consisting of alkyl, alkoxyalkyl, phenyl, substituted phenyl, and optionally substituted heteroaryl.

69. A compound according to Claim 68, wherein R_b is 4-methylphenylthio or 2-pyridinylthio.

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70. A compound according to Claim 9, wherein



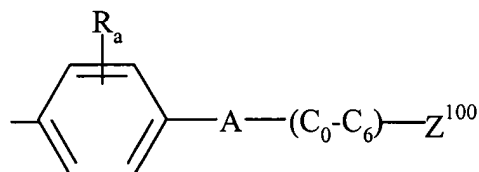
R_1 is

where Z^{100} is selected from the group consisting of benzo[b]thiophene, furanyl and thiophene.

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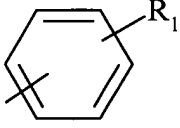
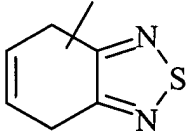
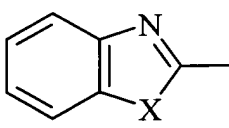
71. A compound according to Claim 9C, wherein R_a is alkoxy; A is $-\text{NH}-\text{C}(\text{O})-$; and there is a covalent bond between A and Z^{100} .

72. A compound according to Claims 1, 8 or 9, wherein



R_1 is

A is selected from the group consisting of $-\text{N}(\text{R})-\text{C}(\text{O})-\text{N}(\text{R})-$, $-(\text{CH}_2)_n-$, $\text{N}(\text{R})\text{C}(\text{O})\text{N}(\text{R})-$, $-\text{N}(\text{R})-$ and $-\text{N}(\text{R})-\text{SO}_2-$; R is hydrogen or alkyl;

Z^{100} is , , , pyridinyl, thiazolyl, furanyl, benzofuranyl or oxazolyl;

- 15 X is S, O or NR where R for each occurrence is independently H or Me; R_a is one or more substituents each independently selected from the group consisting of H and F; and R_b is one or more substituents each independently selected from the group consisting of H, F, Cl, Br, NO_2 , CF_3 , alkyl, alkoxy and alkoxycarbonyl.

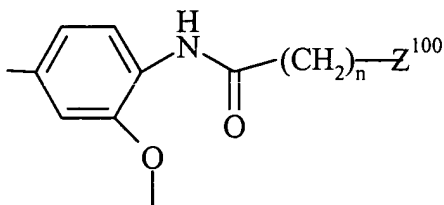
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73. A compound according to Claim 72, wherein R_4 is methyl; m is 1, 2 or 3; R_5 is Y-Z, where Y is $-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})-$ or $-\text{C}(\text{O})-(\text{CH}_2)_p-$; and Z is aminoalkyl, N-alkylamino, N,N-dialkylamino or

hydroxyalkylaminoalkyl.

74. A compound according to Claim 9, wherein

R_4 is methyl; R_1 is

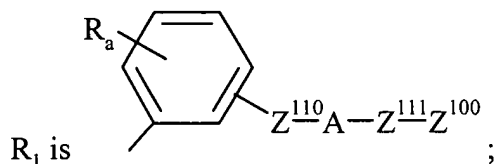


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where n is 0 to 3; Z^{100} is an optionally

substituted group selected from the group consisting of indolyl, indenyl, methylindenyl, methylindolyl, dimethylaminophenyl, phenyl, cyclohexyl and benzofuranyl.

10 75. A compound according to claim 9, wherein



Z^{100} is an optionally substituted group selected from the group consisting of phenyl, imidazolyl, indolyl, furanyl, benzofuranyl and 2,3-dihydrobenzofuranyl;

where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, Cl, CN, optionally substituted alkyl, -O-(optionally substituted alkyl), -COOH, - Z^{105} -C(O)N(R)₂, - Z^{105} -N(R)-C(O)- Z^{200} , - Z^{105} -N(R)-S(O)₂- Z^{200} , and - Z^{105} -N(R)-C(O)-N(R)- Z^{200} ;

15

Z^{105} is a covalent bond or (C₁-C₆);

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Z^{200} is an optionally substituted group selected from group consisting of (C₁-C₆), phenyl and -(C₁-C₆)-phenyl;

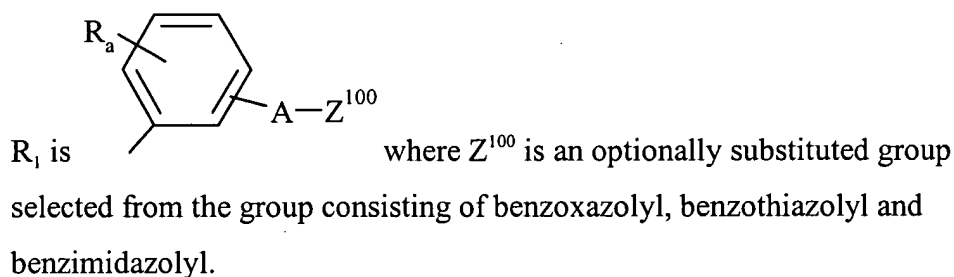
Z^{110} and Z^{111} are each independently a covalent bond or (C₁-C₃) group optionally substituted with alkyl, hydroxy, COOH, CN or phenyl; and

A is O, -N(R)-C(O)-N(R)-, -N(R)-C(O)-O-, -N(R)- or -N(R)-C(O)-, where R is H or alkyl.

76. A compound according to Claim 75, wherein R_4 is methyl.

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77. A compound according to Claim 8, 9 or 10, wherein

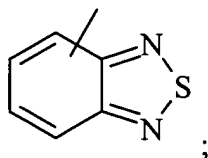
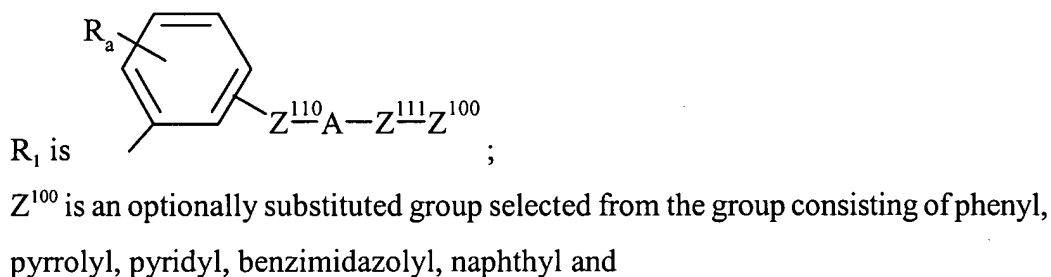


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78. A compound according to Claim 77, wherein R_4 is methyl; A is -NH-; there is only one R_a and it is H or F; and Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of alkyl, halo, CF_3 , and alkoxy.

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79. A compound according to Claim 9, wherein



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where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, Cl, Br, NO_2 , amino,

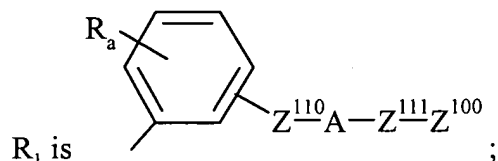
N-alkylamino, N,N-dialkylamino, CN, optionally substituted alkyl, -O-(optionally substituted alkyl) and phenyl;

Z^{110} and Z^{111} for each occurrence is independently (C_0 - C_3) optionally substituted with optionally substituted phenyl; and

5 A is -N(R)-C(O)-N(R)-, -N(R)-S(O)₂-, -N(R)-C(O)-, -N(R)- or -N(R)-C(O)-O-.

80. A compound according to Claim 79, wherein R_4 is methyl and there is only one R_a and it is F.

10 81. A compound according to Claim 9 or 66, wherein



Z^{100} is an optionally substituted group selected from the group consisting of phenyl, isoxazolyl, tetrahydronaphthyl, furanyl, benzofuranyl, pyridyl and indolyl;

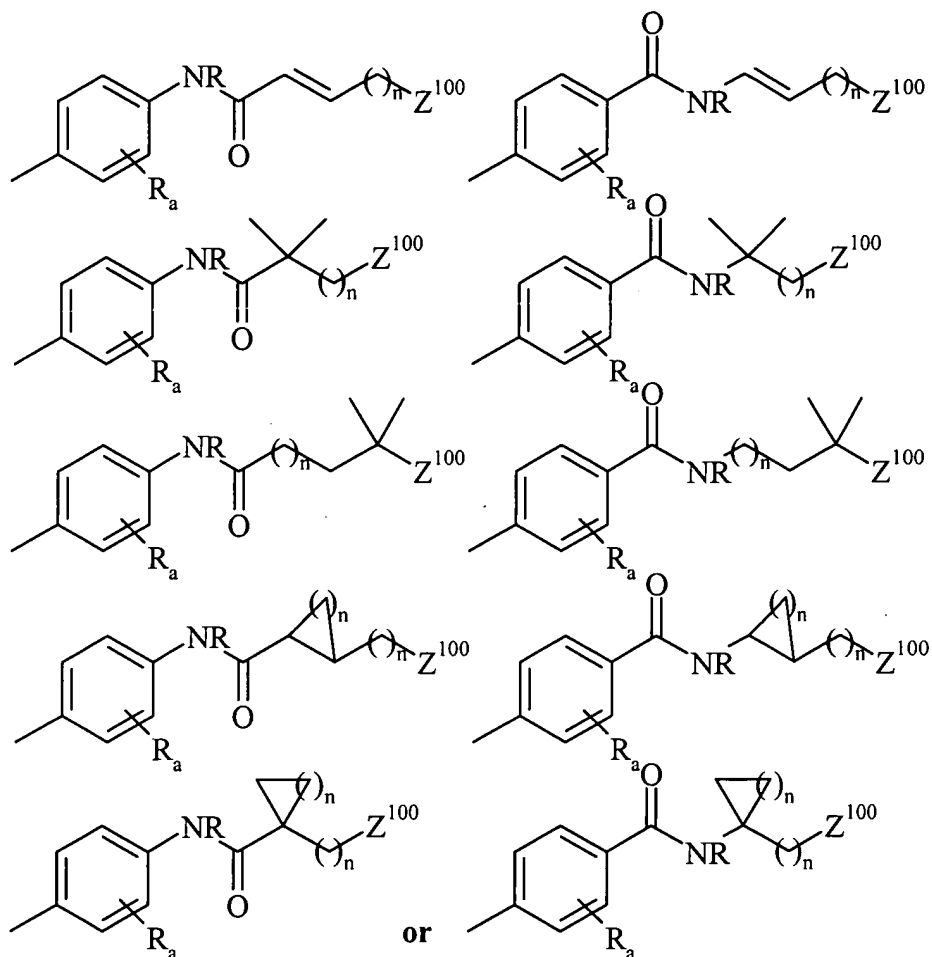
15 where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, CN, NO₂, -C(O)H, -CONH₂, -NHSO₂CF₃, optionally substituted alkyl, optionally substituted heteroaryl and -O-(optionally substituted alkyl);

Z^{110} and Z^{111} are each independently optionally substituted (C_0 - C_3); and

20 A is O, -N(R)-C(O)-(CH₂)_n-N(R)-, -C(O)-N(R)-, -N(R)-C(O)-O-, -N(R)-C(O)- or -N(R)-.

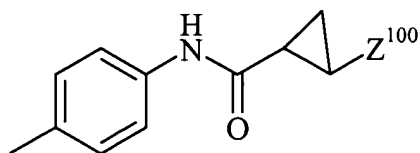
82. A compound according to Claim 81, wherein R_4 is methyl; R_a is H or methoxy; and Z^{110} and Z^{111} are each unsubstituted.

83. A compound according to Claim 9, wherein R_1 is



where R is H or lower alkyl and n is for each occurrence is independently 1 to 6.

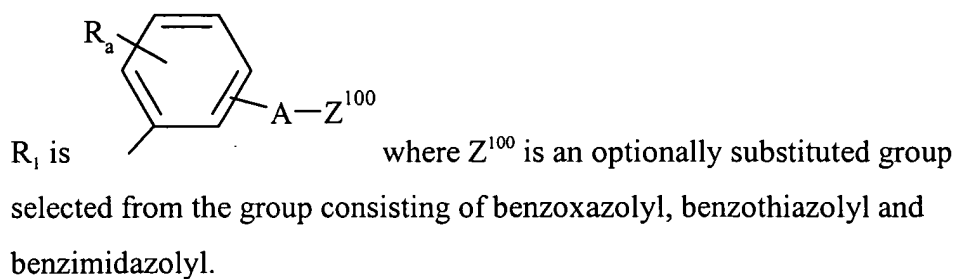
84. A compound according to Claim 83, wherein R_1 is



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85. A compound according to Claim 84, wherein Z^{100} is substituted or unsubstituted phenyl.

- 10 86. A compound according to Claim 8, 9 or 10, wherein



- 5 87. A compound according to Claim 11 wherein n is 2; R_6 is H; m is 1; r is 1; and R_4 and R_5 are each hydrogen.
88. A compound according to claim 64 or 87 wherein R_1 is 4-phenoxyphenyl.